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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,594	11/28/2005	Marc Blondel	0070663-000002	1460

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/531,594	BLONDEL ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11-22* is/are pending in the application.

4a) Of the above claim(s) *1-8,11-13 and 15* is/are withdrawn from consideration.

5)☒ Claim(s) *16,17 and 22* is/are allowed.

6)☒ Claim(s) *14 and 18-21* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 9/23/2010, are acknowledged and entered.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/23/2010 has been entered.

Election/Restrictions

Claims 16-17 and 22 are allowable. The restriction requirement between the product and process claims, as set forth in the Office action mailed on 2/25/2008, has been reconsidered in view of the allowability of claims to the elected invention pursuant to MPEP § 821.04(a). **The restriction requirement is hereby withdrawn as to any claim that requires all the limitations of an allowable claim.** Claims 14 and 18-21, directed to methods of treatment comprising administration of a composition as recited in allowable claims 16 or 17 are no longer withdrawn from consideration because the claim(s) requires all the limitations of an allowable claim. However, claims 1-8, 11-13, and 15, directed to kits, methods of screening, and methods of treatment remain withdrawn from consideration because the claim(s) do not require all the limitations of an allowable claim.

In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Response to Arguments

Applicants' arguments, filed 9/23/2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

Claim 14 is objected to because of the following informalities: the claim depends from withdrawn claim 13. Appropriate correction is required.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention.", (see MPEP § 2173).

Claims 14 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The patient population(s) of claims 14 and 18-20 is not clearly defined in the claims. Claim 14 depends from withdrawn claim 13, which recites the limitation "administering the compound of formula (II). However, the active method step of the claim is not so linked to the preamble of the claim so as to clearly and unequivocally convey that the administration is to a subject having a neurodegenerative disease. With regard to claims 18-20, the recited "method of treatment" comprising the administration "to a patient in need thereof" does not define what is being treated. Further, it is not clear whether the "patient in need thereof" is a patient in need of "treatment" or any patient "in need of" the composition of claim 16.

Claim Rejections - 35 USC § 112 – 1st Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 18-21 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to

practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing Ex parte Forman, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, and breadth of the claims

The invention is drawn to methods of "treatment" (no patient populations defined in the claims) and to methods of treating neurodegenerative diseases comprising administration of a compound of Formula (II) as defined in claims 14 and 16. As disclosed by Applicants, neurodegenerative diseases include spongiform encephalopathies, Alzheimer's disease, Parkinson's disease, and Huntington's disease.

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not

The state and predictability of the art, and relative skill of those in the art

As a general rule, enablement must be commensurate with the scope of claim language. MPEP 2164.08 states, "The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to **make and use the full scope of the claimed invention** without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)" (emphasis added). The "make and use the full scope of the invention without undue experimentation" language was repeated in 2005 in Warner-Lambert Co. v. Teva Pharmaceuticals USA Inc., 75 USPQ2d 1865, and Scripps Research Institute v. Nemerson, 78 USPQ2d 1019 asserts: "A lack of enablement for the full scope of a claim, however, is a legitimate rejection." The principle was explicitly affirmed most recently in *Auto. Tech. Int'l,* Inc. v. BMW of N. Am., Inc., 501 F.3d 1274, 84 USPQ2d 1108 (Fed. Cir. 2007), Monsanto Co. v. Syngenta Seeds, Inc., 503 F.3d 1352, 84 U.S.P.Q.2d 1705 (Fed. Cir. 2007), and Sitrick v. Dreamworks, LLC, 516 F.3d 993, 85 USPQ2d 1826 (Fed. Cir. 2008). See also In re Cortright, 49 USPQ2d 1464, 1466 and Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer Inc., 49 USPQ2d 1370.

By way of background, four cases are of particular relevance to the question of enablement of methodd of treating diseases broadly or even generally:

In In re Buting, 57 CCPA 777, 418 F.2d 540, 163 USPQ 689, the claim was drawn to "The method of treating a malignant condition selected from the group consisting of leukemias, sarcomas, adenocarcinomas, lymphosarcomas, melanomas, myelomas, and ascitic tumors" using a small genus of compounds. The Court decided that human testing "limited to one compound and two types of cancer" was not "commensurate with the broad scope of utility asserted and claimed".

In Ex parte Jovanovics, 211 USPQ 907 the claims were drawn to "the treatment of certain specified cancers in humans" by the use of a genus of exactly two compounds, the N-formyl or N-desmethyl derivative of leurosine. Applicants submitted "affidavits, publications and data" for one of the compounds, and a dependent claim drawn to the use of that species was

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"experimentation".

allowed. For the other, no data was presented, applicants said only that the other derivative would be expected to be less effective; claims to the genus were refused.

In Ex parte Busse, et al., 1 USPQ2d 1908, claims were drawn to "A therapeutic method for reducing metastasis and neoplastic growth in a mammal" using a single species. The decision notes that such utility "is no longer considered to be "incredible", but that "the utility in question is sufficiently unusual to justify the examiner's requirement for substantiating evidence. Note also that there is also a dependent claim 5 which specified "wherein metastasis and neoplastic growth is adenocarcinoma, squamous cell carcinoma, melanoma, cell small lung or glioma." The decision notes that "even within the specific group recited in claim 5 some of the individual terms used actually encompass a relatively broad class of specific types of cancer, which specific types are known to respond quite differently to various modes of therapy."

In Ex parte Stevens, 16 USPQ2d 1379 a claim to "A method for therapeutic or prophylactic treatment of cancer in mammalian hosts" was refused because there was "no actual evidence of the effectiveness of the claimed composition and process in achieving that utility."

While the claims in the above cases were drawn to treating cancer, the holdings in these cases are pertinent to the instant claims, which are drawn to the treatment of any patient or to the treatment of patients having any neurodegenerative disease.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. That factor is outweighed, however, by the unpredictable nature of the art.

It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), Nationwide Chemical Corporation, et al. v. Wright, et al., 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), Ex parte Sudilovsky 21 USPQ 2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) In re Wright 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that

success in developing specific avian recombinant virus vaccine was uncertain). As long as the Specification discloses at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112, 1st Paragraph is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). To that extent, if little is known in the prior art about the nature of the invention and the art is unpredictable, the Specification would need more detail as to how to make and use the invention in order to be enabling. See Chiron Corp v. Genetech, lnc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching. The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology.")

In the instant case, there is no evidence of record of analogous compounds having efficacy in the treatment of any disease or condition, including neurodegenerative diseases. There is no evidence of record that any compound of the invention has any efficacy in the treatment of any disease or condition in a patient.

The amount of direction or guidance provided and the presence or absence of working examples

The specification is directed to screening assays and kits for identifying inhibitors of prion activity. The claimed compounds have been shown to exhibit some anti-prion activity by these screens. The tests are in vitro and do not involve testing with animal models of any type of disease.

The specification lacks information related to what the claimed compounds may be effective for treating. Claims drawn to methods of administering said compositions to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments. In particular, prion-related diseases are not well understood and there is no treatment for them. The specification is directed to screening assays. The specification fails to provide guidance that would enable a person of skill in the art to determine which prion-related maladies could be treated by a pharmaceutical composition of the elected compounds.

Applicants have previously argued (see response filed 3/24/2009) in response to an enablement rejection against the claimed compositions that the in vitro tests of the present invention (yeast-based assay) correlate with the claimed methods. Applicants further argued that the tests and supporting data of the instant specification are sufficient and reliable indicators of a biological activity of such compounds and are reasonably predictive that such compounds would be useful for treating prion-associated pathologies.

The Examiner is not convinced that Applicants have enabled one skilled in the art to use the claimed compositions for the treatment of patients or for the treatment of neurodegenerative diseases. Firstly, Applicants have presented no evidence of record that the in vitro and in vivo tests of anti-prion activity disclosed in the specification are known to be predictive of the treatment of, for example, Alzheimer's disease or Parkinson's disease. Secondly, as discussed in the Office Action mailed 7/16/2009, Groshup (2008) teaches that most factors which modulate the pathogenesis of prion infection in vivo are still an enigma (page 9/13, 1st full paragraph). Similarly, Zou (2004) makes similar observations regarding the usefulness of in vitro and in vivo models of human prion diseases and notes that "Although the animal models appear potentially helpful in further characterizing phenotypes of human prion diseases upon passage to animals, great caution must be exercised before equating the disease phenotype produced in an animal model with that of the modeled human disease" (p. 162, penultimate paragraph).

Thus, one can conclude that in vitro results do not predictably correlate with in vivo models or in humans suffering from a prion disease. In vivo studies with "accepted" mouse models do not correlate with human results. Hence, there is a very high degree of unpredictability regarding correlation between or among the various in vitro and in vivo mouse models and human experience with quinacrine which is known to pass through the human blood-brain barrier (Geschwind (2008) page 531, first sentence of first full paragraph).

The specification is directed to screening assays. The correlation among in vitro, yeast-based assays and in vivo mouse models with human efficacy for treatment of prion disease is highly unpredictable. The specification fails to provide guidance that would enable a person of skill in the art to determine which prion-related maladies could be treated by a pharmaceutical composition of the elected compounds.

The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed supra) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed genus of compounds could be predictably used as a "treatment" for patients as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In the instant case, Applicants have presented a general idea that because three of the instantly claimed compounds have anti-prion activity in vitro and in vivo in screening assays then all compounds of Formula (II) as defined in the instant claims must therefore, a priori, be useful in the "treatment" of patients, including the treatment of any and all neurodegenerative diseases.

Determining if any particular claimed compound would treat any particular disease state would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants. As noted supra, even in vitro and in vivo assays of anti-prion activity do not predictably correlate to efficacy in treating any disease in humans and are not generally predictive of clinical efficacy.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Allowable Subject Matter

Claims 16-17 and 22 are allowed.

The following is a statement of reasons for the indication of allowable subject matter: the prior art does not teach or suggest pharmaceutical compositions comprising a compound of

Formula (II) as defined in the instant claims. Applicants have enabled one skilled in the art to use such pharmaceutical compositions for screening compounds for anti-prion activity.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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